

# **A New “Hybrid”?: Combining Elements of Clinical Effectiveness and Implementation Research Trials**

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## **Session Outline**

- Why these hybrids?
- Some definitions and thoughts on clinical efficacy, clinical effectiveness, and implementation research
- Research “Pipelines” then and now
- Hybrid effectiveness-implementation research:
  - A proposed typology (more about why...)
  - Rationale of the Types
  - Design challenges and trade-offs
- Ecological challenges
- Wrap-up and onward to the exercise



## Why *These* Hybrids?

- Let's "cut to the chase" shall we?
  - **Main reason:** To speed the process from the development of clinical knowledge to lots of people using it
  - **Also:** To "backfill" knowledge that we were in too much of a hurry to gain first (we'll explain a bit later...)



## Some Terms Defined

- **Hybrid:** Something of mixed origin or composition
- **Dissemination:** Passive spread of information or use of an [evidence-based] innovation
  - Cf. "targeted distribution of information" (NIH PA)
- **Implementation:** "Efforts designed to get evidence/best practice findings and related products into use via appropriate change/uptake/adoption interventions" (QUERI Glossary)



## More Terms Defined...

- **Clinical\* Intervention:** Clinical initiative, manipulation, change to be introduced into a healthcare venue
  - E.g.: collaborative care for depression, early aspirin for MI
- **Implementation Intervention:** “A single method or technique to facilitate change” (QUERI Glossary)
  - E.g.: automated clinical reminder, performance feedback
- **Implementation Strategy:** “An integrated set, bundle, or package of [implementation] interventions” (QUERI Glossary)

\*Includes *health promotion* and *delivery system* interventions also...



## Clinical Efficacy, Effectiveness...

- **Clinical Efficacy Research:** Focused on limited clinical/symptom outcomes at the Pt. level, internal validity, isolates impact of clinical intervention, “ideal conditions”, smaller selected samples
- **Clinical Effectiveness Research:** Focused on clinical and QoL outcomes, also public health impact, external validity, “real world” settings, larger and more diverse samples
- **Key Issues:**
  - Efficacy-Effectiveness & IV-EV are ends of a **spectrum**, not alternate categories
  - Moving along the spectrum requires **trade-offs**: Every design decision is a deal with the devil...



# Implementation Research

- **Implementation Research:** Focus on *uptake* of clinical interventions, outcomes are usually clinic/provider behaviors (e.g., rates of adoption), implementation research trials test implementation interventions or strategies
  - Can there be *efficacy* and *effectiveness* trials in implementation research? **Yes**, we'll touch on this a little later
  - In standard implementation trials, clinical outcomes data are not needed because suitable clinical efficacy and effectiveness data have already been collected and disseminated (e.g., guidelines)



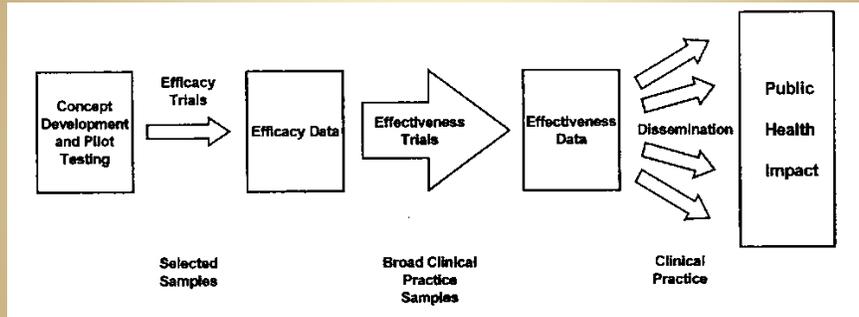
## Clinical vs. Implementation Trial Designs (“traditional”)

Design Characteristic	Clinical Focus	Implementation Focus
The Manipulation	Clinical Intervention	Implementation Intervention
Outcome	Symptoms, Health Outcomes	Adoption, Sustained Uptake, Fidelity
Typical Unit of Analysis	Patient	Site, Clinic, Provider
Typical Randomization	Patient	Site, Provider (or Non- Randomized)
Formative Evaluation*	None	Typically
Qualitative Data	Sometimes, but secondary	Typically

\*We'll define this in a minute...



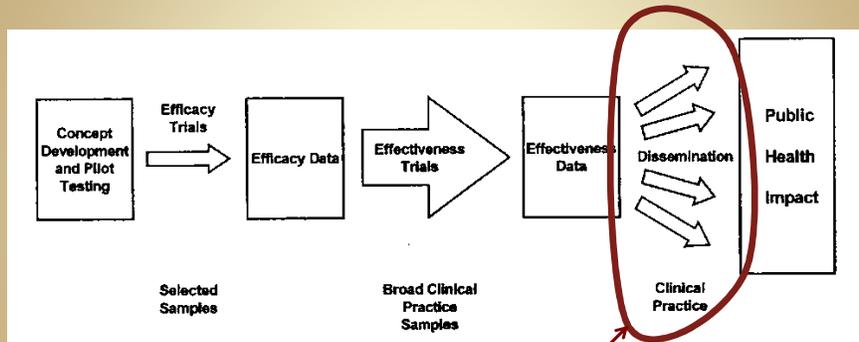
# The Landscape ~ 10 Years Ago



from Bauer, 2001



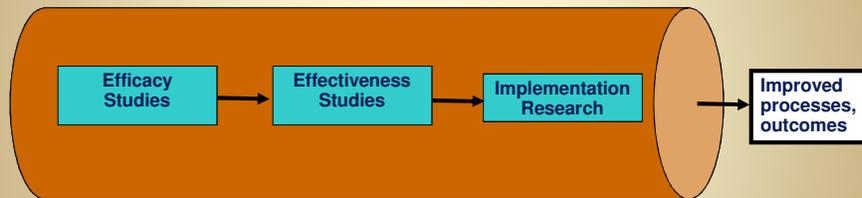
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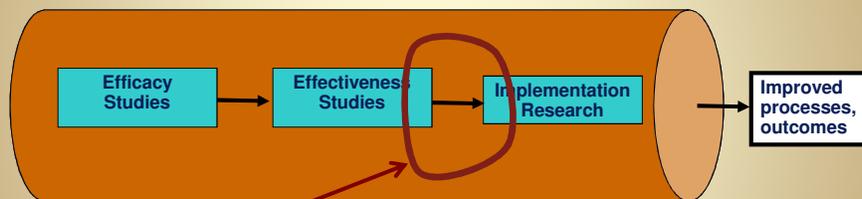
**"Implementation Research" goes in here now...**



## “Newer” Clinical Research-Implementation Pipeline



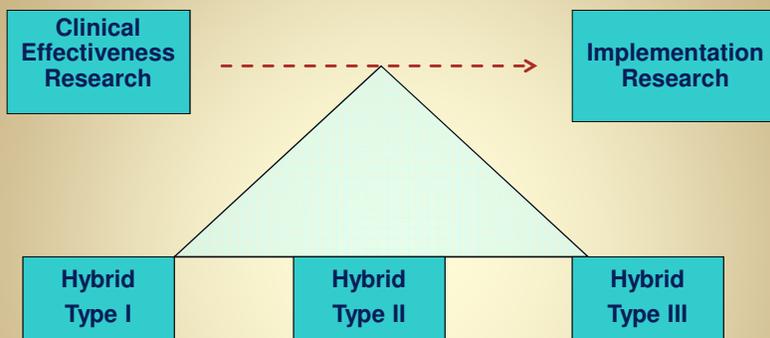
## “Newer” Clinical Research-Implementation Pipeline



*Spatially speaking, our Hybrids “go” in here...*



## First Look at the Types



**Hybrid Type I:**  
test clinical intervention, observe/gather information on implementation

**Hybrid Type II:**  
test clinical intervention, test implementation intervention

**Hybrid Type III:** test implementation intervention, observe/gather information on clinical intervention and outcomes



## Another Look...

	Intervention Focus	Implementation	
		Yes	No
Clinical	Yes	Hybrid Type II	Hybrid Type I
	No	Hybrid Type III	Observational Research

**Hybrid Type I:** test clinical intervention, observe/gather information on implementation

**Hybrid Type II:** test clinical intervention, test implementation intervention

**Hybrid Type III:** test implementation intervention, observe/gather information on clinical intervention and outcomes

(We'll discuss *randomization* a bit later...)



## More In-Depth: Hybrid Type 1

- **Definition (again):** test clinical intervention, observe/gather information on implementation
- **Rationale/Description**
  - Facilitates more rapid transition to implementation research
  - Only modest refinements to clinical effectiveness studies are necessary
  - Including *process evaluations* of implementation during clinical effectiveness trials can provide valuable information to subsequent implementation research trials.



## Hybrid Type 1 (cont.)

- **Process evaluation accompanying clinical effectiveness trial:**
  - Potential barriers/facilitators to implementation during the clinical effectiveness trial?
  - Ability of clinic staff to implement the clinical protocol?
  - Gather information on potential modifications (to clinical intervention or implementation assistance) during the trial to make it more adoptable
- **What other approaches could you think of?**



## More In-Depth: Hybrid Type 2

- **Definition (again):** test clinical intervention, test implementation intervention
- **Rationale/Description**
  - “Two birds with one stone” under right conditions
    - Effectiveness trial does not need to be huge?
    - Right time for small-scale implementation study?
    - Cooperative sites?
  - Two “sets” of outcomes data are collected: **clinical** (patient-level) and **implementation** (site, clinic, provider...)



## Hybrid Type 2 (cont.)

- **More Rationale/Description**
  - Implementation research likely to be preliminary, e.g., feasibility pilot or small-scale efficacy-like trial
  - **Formative Evaluation** extremely likely for implementation intervention
    - What barriers or problems emerge after implementation begin?
    - What changes to implementation intervention/strategy could be done now to improve uptake?
    - Are any parts of the implementation strategy unnecessary?
    - **What other questions could a FE look into here?**



## Formative Evaluation (FE)

- “A rigorous assessment process designed to identify potential and actual influences on the progress and effectiveness of implementation efforts. [Designed to occur] ...before, during, and after implementation to optimize the potential for success.” (Stetler et al., 2006)
- Data are used concurrently, e.g., to tailor to resolve barriers



## More In-Depth: Hybrid Type 3

- **Definition (again):** test implementation intervention, observe/gather information on clinical intervention and outcomes
- **Rationale/Description**
  - We sometimes proceed with implementation studies without completing the full portfolio of effectiveness studies
  - In these cases we should seek to collect evidence of clinical effectiveness under the (likely) novel conditions/settings of the implementation trial
  - More feasible and attractive when clinical outcomes data are more widely available



## Likely Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
Research Aims	<p><b>Primary Aim:</b> Determine effectiveness of a clinical intervention</p> <p><b>Secondary Aim:</b> Better understand context for implementation</p>	<p><b>Primary Aim:</b> Determine effectiveness of a clinical intervention</p> <p><b>Secondary Aim:</b> Determine feasibility and/or potential efficacy of an implementation intervention</p>	<p><b>Primary Aim:</b> Determine efficacy or effectiveness of an implementation intervention</p> <p><b>Secondary Aim:</b> Assess clinical outcomes associated with implementation trial</p>



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
Research Questions (examples)	<p><b>Primary Question:</b> Will a clinical treatment work in this setting/these patients?</p> <p><b>Secondary Question:</b> What are potential barriers/ facilitators to a treatment's implementation?</p>	<p><b>Primary Question:</b> Will a clinical treatment work in this setting/these patients?</p> <p><b>Secondary Question:</b> Does the implementation method show promise (either alone or in comparison to another method)?</p>	<p><b>Primary Question:</b> Which method works better in facilitating implementation of a clinical treatment?</p> <p><b>Secondary Question:</b> Are clinical outcomes acceptable for this population?</p>



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
<b>Units of Randomization</b>	Patient (most common perhaps)*	<p><b>Variant A</b> (<i>clinical effectiveness trial with non-randomized implementation study</i>): Patient*</p> <p><b>Variant B</b> (<i>dual randomized trial</i>): Patient* for clinical treatment <i>and</i> Clinic/Provider* for implementation (factorial design)</p>	Clinic/Provider* for implementation

\* could be facility, or system, etc.



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
<b>Comparison Conditions</b>	Placebo, treatment as usual, competing treatment	<p><b>Variant A:</b> Patient = Placebo, treatment as usual, competing treatment</p> <p><b>Variant B:</b> Patient = Placebo, treatment as usual, competing treatment; Clinic/Provider = implementation as usual, competing implementation intervention</p>	<b>Clinic/Provider:</b> implementation as usual, competing implementation intervention



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
<b>Evaluation Methods</b>	<p><b>Primary Aim:</b> quantitative, summative</p> <p><b>Secondary Aim:</b> mixed methods, qualitative, process-oriented for clinical intervention</p>	<p><b>Primary Aim:</b> quantitative, summative</p> <p><b>Secondary Aim:</b> mixed methods, process or formative, and summative</p>	<p><b>Primary Aim:</b> quantitative, mixed-method, qualitative, formative and summative</p> <p><b>Secondary Aim:</b> quantitative, summative</p>



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
<b>Measures</b>	<p><b>Primary Aim:</b> Patient symptoms and functioning, possibly cost-effectiveness</p> <p><b>Secondary Aim:</b> Feasibility and acceptability of implementing clinical treatment, sustainability potential, barriers and facilitators to implementation</p>	<p><b>Primary Aim:</b> Patient symptoms and functioning, possibly cost-effectiveness</p> <p><b>Secondary Aim:</b> Adoption of clinical treatment and fidelity to it, sustainability potential, barriers and facilitators to implementation</p>	<p><b>Primary Aim:</b> Adoption of clinical treatment and fidelity to it, sustainability potential, barriers and facilitators to implementation</p> <p><b>Secondary Aim:</b> Patient symptoms, functioning, services use</p>



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
<b>Key Design Challenges</b>	<p>Generating “buy in” among clinical researchers</p> <p>Insuring expertise on study team to conduct Secondary Aim</p> <p>These studies will likely have more research personnel and larger budgets than non-hybrids</p>	<p>Power low for Secondary Aim</p> <p>More research personnel and larger budgets than non-hybrids</p> <p>Insuring appropriate expertise on study team to rigorously conduct both Aims</p>	<p>Primary data collection with patients in large, multi-site implementation trials can be unfeasible</p> <p>Chart review/admin data/kiosk data will not be extensive and might be insufficient to answer some questions.</p>



## More Approach and Design Differences Across Hybrids

Study Characteristic	Hybrid Type I	Hybrid Type II	Hybrid Type III
<b>Key Design Challenges</b>		<p>“Creep” of clinical treatment away from fidelity needed for optimal effectiveness (adaptations going too far)</p> <p>IRB complexities with multiple types of participants</p>	<p>“Creep” of clinical treatment away from fidelity needed for optimal effectiveness.</p> <p>“Creep” of implementation interventions away from evidence base</p> <p>IRB complexities with multiple types of participants</p>



## Some *Ecological* Challenges in Hybrid Research

- Lack of shared concepts, constructs, vocabulary within the field [*see above...*]
- Lack of familiarity, appreciation, impetus for implementation science issues outside of the field
  - Grant reviewer expertise along the spectrum required
  - Editorial interest/expertise among top journals
  - Academic promotion path tougher [*our business case*]
- Lack of familiarity, appreciation, impetus of clinical intervention trials complexities within the implementation field



## So, Again, Tell Me, Why Do Hybrid Research?

(*Implementation research is tough enough...*)

- Speed is of the essence!
- Bidirectionality of flow of information
- Process improvements do not necessarily mean health outcome gains
  - Or: Guideline concordance  $\neq$  patient improvement



## Some closing thoughts...

- Not every study needs to be a hybrid!
- Some hybrids won't be feasible or affordable
- Hybrids and the **QUERI Revised Pipeline**
  - **Hybrid I:** likely located in/between “mainstream” and “Pre-implementation”
  - **Hybrid II:** likely located in/between “implementation planning” and “implementation trial”
  - **Hybrid III:** likely located in “implementation trial”



## Exercise

- Consume the abstract
- Think about how it could be a Hybrid I, II, etc.
- Think about design trade-offs
  - If it were a Hybrid I, what should it look like?
    - How many patients, sites, clinics?
  - If it were a Hybrid II, what should it look like?
    - How many patients, sites, clinics?
  - What outcomes to measure?
  - Could it be a Hybrid III?

